CTFR 11

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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
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EXAMINER	
FORMAN, B	
ART UNIT	**PAPER NUMBER**
1655	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/417,268	CHENCHIK, ALEX	
	Examiner	Art Unit	
	BJ Forman	1655	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

1)☐ Responsive to communication(s) filed on *19 September 2000* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17,53 and 57-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-17,53 and 57-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a)☐ All b)☐ Some * c)☐ None of the CERTIFIED copies of the priority documents have been:

1.☐ received.

2.☐ received in Application No. (Series Code / Serial Number) _____ .

3.☐ received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. & 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

1. This action is in response to papers filed 19 September 2000 in Paper No. 9 in which claims 1, 2, 10, 12, 14-17, 57 and 58 were amended. All of the amendments have been thoroughly reviewed and entered. The previous rejections under 35 U.S.C. 112, second paragraph in the Office Action of Paper No. 8 mailed 16 June 200 are withdrawn in view of the amendments. The previous rejections under 35 U.S.C. 102(e) and 35 U.S.C. 103(a) in the Office Action of Paper No. 8 are maintained. All of the arguments have been thoroughly reviewed and are discussed below.

Currently claims 1-17, 53, and 57-59 are under prosecution.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1, 2, 5-10, 12-17, 57 & 58 are rejected under 35 U.S.C. 102(e) as being clearly anticipated by Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995).

Regarding Claim 1, Brown et al. disclose an array which is a multi-cell substrate, comprising at least one pattern of probe oligonucleotide spots wherein a spot is a "cell" on a multi-cell substrate wherein each "cell" contains a microarray, wherein the spots (microarrays) are attached to the surface of a solid support (Column 11, lines 43-67), wherein each probe oligonucleotide spot (microarray) comprises an oligonucleotide probe composition made up of a plurality of unique oligonucleotides (Column 4, lines 16-19) wherein said plurality comprises 2 or more unique oligonucleotides of different sequence that hybridize to the same target nucleic

acid i.e. all known mutations (different sequence) of a given gene (target nucleic acid (Column 15, lines 22-27).

Regarding Claim 2, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein said plurality of unique oligonucleotides hybridize to different regions of the target nucleic acid wherein the different regions represent all known mutations in a disease gene (Column 15, lines 19-27).

Regarding Claim 5, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein two or more different target nucleic acids are represented in said pattern (Column 4, lines 52-55).

Regarding Claim 6, Brown et al. disclose the array (multi-cell substrate) wherein each oligonucleotide spot (microarray) corresponds to a different target nucleic acid i.e. different target yeast nucleic acids are arrayed in different spots (microarrays) of the array (Example 3, Column 18, lines 39-43).

Regarding Claim 7, Brown et al. disclose the array (multi-cell substrate) of Claim 5 wherein two or more oligonucleotide spots (microarray) correspond to the same target nucleic acid (Column 13, lines 1-10).

Regarding Claim 8, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein said array comprises a plurality of said patterns of oligonucleotide spots (microarray) (Column 11, lines 51-58).

Regarding Claim 9, Brown et al. disclose the array (multi-cell substrate) of Claim 8 wherein said plurality of patterns are separated from each other by walls which are grids (Column 4, lines 45-51).

Regarding Claim 10, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein each of said oligonucleotides range from 15 to 150 nucleotides in length (Column 13, lines 21-22).

Regarding Claim 12, Brown et al. teach the array (multi-cell substrate) of Claim 1 wherein the oligonucleotide probe composition comprises about 3 to 50 oligonucleotides i.e. each oligonucleotide probe spot (microarray) has a size of $1mm^2$ (Column 11, line 62-67) and a probe density of 100 per cm^2 (Column 6, lines 32-33).

Regarding Claim 13, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein all of the oligonucleotide spots hybridize to the same type of target nucleic acid i.e. cDNA (Column 4, lines 60-64).

Regarding Claim 14, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the density of spots (microarray) on said array does not exceed about $1000/cm^2$ (Column 11, lines 62-67).

Regarding Claim 15, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the density of spots (microarray) on said array does not exceed about $400/cm^2$ (Column 11, 62-67).

Regarding Claim 16, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the number of spots (microarray) on said array ranges from about 50 to 10,000 i.e. 96 (Column 11, 62-67).

Regarding Claim 17, Brown et al. disclose the array (multi-cell substrate) of Claim 1 wherein the number of spots (microarray) on said array ranges from about 50 to 1,000 i.e. 96 (Column 11, 62-67).

Regarding Claim 57, Brown et al. teaches an array which is a multi-cell substrate, comprising a pattern of probe oligonucleotide spots which are microarrays, that are attached to a surface of a solid support (Column 11, lines 51-61) wherein each probe oligonucleotide spot (microarray) comprises an oligonucleotide probe composition made up of 3 to 50 unique oligonucleotides (Column 6, lines 32-33 and Column 11, line 62-67) of from about 15 to 150 nucleotides in length (Column 13, lines 21-22) and wherein each unique oligonucleotide hybridizes to a different region of the target nucleic acid (Example 3, Column 18, lines 40-43).

Regarding Claim 58, Brown et al. teaches an array which is a multi-cell substrate, comprising a pattern of probe oligonucleotide spots which are microarrays, that have a density that does not exceed about 400 spots (microarray)/cm^2 attached to a surface of a solid support (Column 11, lines 62-67) wherein each probe oligonucleotide spot (microarray) corresponds to a different target nucleic acid (Example 3, Column 18, lines 40-43) and comprises an oligonucleotide composition made up of 3 o 20 unique oligonucleotides (Column 6, lines 32-33 and Column 11, line 62-67) of from about 25 to 100 nucleotides in length (Column 13, lines 21-22) wherein each unique oligonucleotide hybridizes to a different region of the target nucleic acid (Example 3, Column 18, lines 40-43).

Response to Arguments

4. Applicant argues that Brown et al. fail to teach an array on which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid. This argument is not found persuasive because as cited above, Brown et al. clearly discloses the array of Claims 1, 2, 5-10, 12-17 and 57-58 wherein each oligonucleotide spot contains two or more different probe of different sequence that hybridize to the same target nucleic acid. Specifically, Brown et al. disclose an array comprising probe spots, wherein a spot is a "cell" on a multi-cell substrate, wherein each "cell" contains a microarray, wherein each spot (microarray) contains two or more different oligonucleotides that hybridize to the same target nucleic acid i.e. fragments representing all known mutations of a given gene as claimed (Column 15, lines 22-27).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. Claims 3-4 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to claim 1 above, and further in view of Fodor et al. (U.S. Patent No. 5,800,992, filed 25 June 1996).

Regarding Claim 3, Brown et al. disclose the array (multi-cell substrate) of Claim 1 comprising at least one pattern of probe oligonucleotide spots (microarray) attached to a surface of a solid support wherein each oligonucleotide spot (microarray) comprises a plurality of unique oligonucleotides for a target nucleic acid. Additionally, Brown et al. teach the unique oligonucleotides are positioned at known addressable regions (Column 11, lines 55-58) and hybridize to all known mutations in a disease gene (Column 15, lines 19-22). Brown et al. do not teach said plurality of unique oligonucleotides hybridize to non-overlapping regions of said target nucleic acid. However, Fodor et al. teach a similar microarray comprising a pattern of unique oligonucleotide probes attached to a surface of a solid support wherein the probes are attached to the support in a matrix of positionally defined regions (Column 2, lines 34-40) and wherein the oligonucleotide probes for fingerprinting hybridize with "absolute complementary matching" to the target sequence (Column 9, lines 60-67).

Regarding Claim 4, Brown et al. do not teach said plurality of unique oligonucleotides hybridize to overlapping regions of said target nucleic acid. However, Fodor et al. teach a similar microarray wherein the oligonucleotide probes for mapping hybridize to overlapping regions of a target nucleic acid (Column 10, lines 1-12). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Brown et al. with the teaching of Fodor et al. to obtain the claimed invention because one of skill in the art would have been motivated with a reasonable expectation of success to modify the oligonucleotide probes of Brown et al. with the oligonucleotide probes of Fodor et al. wherein both sets of probes are used in hybridization assays, based on the oligonucleotide probes' equivalent chemical and physical properties and the oligonucleotide probes' equivalent positioning on the substrate and based on experimental design wherein overlapping probes are

used for mapping and non-overlapping probes are used for fingerprinting for the expected benefit of rapid and convenient screening, eliminating the need to handle and detect individual arrays as taught by Brown et al. (Column 15, lines 59-64).

Response to Arguments

7. Applicant argues that Brown et al. fail to teach an array on which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and that the teaching of Fodor et al. fails to make up the deficiency of Brown et al. such that the combined teaching fail to teach or suggest the claimed probe composition. This argument is not found persuasive because as cited above, Brown et al. clearly discloses the claimed probe spot composition (Column 15, lines 19-27).

8. Claim 11 is rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to Claim 1 and further in view of Lockhart et al. (U.S. Patent No. 6,040,138, filed 15 September 1995).

Regarding Claim 11, Brown et al. do not teach the array (multi-cell substrate) of Claim 1 wherein the array further comprises at least one mismatch probe. However, Lockhart et al. teach a similar microarray comprising a pattern of unique oligonucleotide probes attached to a surface of a solid support wherein the probes are attached to the support in a matrix of positionally defined regions (Column 2, lines 60-65) and wherein the microarray comprises at least one mismatch probe (Column 3, line 30). It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to modify the array of Brown et al. with the teaching of Lockhart et al. to obtain the claimed invention because one skilled in the art would have been motivated with a reasonable expectation of success modify the Brown et al. microarray of probes and to include mismatch control probes as taught by Lockhart et al. wherein hybridization signal intensity is compared to mismatch hybridization for the expected benefit of accurately quantifying hybridization as taught by Lockhart et al. (Column 3, lines 30-38).

Response to Arguments

9. Applicant argues that Brown et al. fail to teach an array on which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and that the teaching of Lockhart et al. fails to make up the deficiency of Brown et al. such that the combined teachings fail to teach or suggest the claimed probe composition. This argument is not found persuasive because as cited above, Brown et al. clearly discloses the claimed probe spot composition (Column 15, lines 19-27).

10. Claims 53 & 59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 5,807,522, filed 7 June 1995) as applied to claim 1 above, and further in view of Stratagene catalog (1989, page 39).

Regarding Claim 53, Brown et al. teach the array of Claim 1 comprising at least one pattern of probe oligonucleotide spots which are microarrays are attached to a surface of a solid support wherein each oligonucleotide spot (microarray) comprises a plurality of unique oligonucleotides for a target nucleic acid. Additionally, they teach hybridization assay and assay reagents wherein the assay is performed on said array (Example 3, Column 18, lines 34-63). Brown et al. do not teach the combined into a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

Regarding Claim 59, Brown et al. teach the hybridization assay further comprising reagents for generating a labeled target nucleic acid sample (Column 16, lines 39-54). Brown et al. do not teach the combined into a kit. Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine the method of Brown et al. into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents

have been assembled and pre-mixed specifically for a defined set of experiments. 2) The other service provided in a kit is quality control" (page 39, column 1).

Response to Arguments

11. Applicant argues that Brown et al. fail to teach an array on which each probe spot includes two or more different oligonucleotides of different sequence that hybridize to the same target nucleic acid and that the motivation to combine reagents into a kit taught by Stratagene fails to make up the deficiency of Brown et al. such that the combined teachings fail to teach or suggest the claimed kit. This argument is not found persuasive because as cited above, Brown et al. clearly discloses the claimed probe spot composition (Column 15, lines 19-27).

12. THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (703) 306-5878. The examiner can normally be reached on 6:45 TO 4:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones can be reached on (703) 308-1152. The fax phone numbers for the

organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-8724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

BJ Forman, Ph.D.
October 13, 2000